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Extraction Efficiency of Extracellular MRI Contrast Agents and Its Model-Dependent Effects on Estimates of Myocardial Blood Flow

In their recent study, Cullen et al. (1) report on the highly relevant determination of a perfusion reserve index with magnetic resonance imaging (MRI) in patients with coronary artery disease. Without wanting to detract from the fact that theirs is a valuable study, we take issue with the negative appraisal of first-pass imaging with rapid bolus injections.

Based on numerous studies with extravascular and intravascular MRI contrast agents it has been shown that the best sensitivity to changes in myocardial blood flow is observed with a rapid bolus injection and imaging during the initial wash-in of contrast agent (2). The investigators suggest that a slower injection and a correspondingly lower temporal resolution (the authors report acquisition of an image every six heart beats) are of practical advantage. In fact, this forces them to determine blood flow indirectly with the Kety model by measuring the product of extraction efficiency (E) and myocardial blood flow (F) and to assume that the extraction efficiency is unchanged for different pathologies. The Kety model is most suitable for modeling the kinetics of freely diffusible tracers because the extraction efficiency can then be set to unity. For extracellular MRI contrast agents such as Gd-DTPA, which are barrier-limited, the assumption that the extraction remains constant is controversial. Several investigators have shown that E varies with flow, and between normal and ischemic/reperfused myocardium by as much as 100% (3,4). Data by Watson et al. (5) comparing the FE product with blood flows measured by positron emission tomography (PET) show that at low flows the FE product is rather insensitive to changes in flow. Furthermore, E is generally not constant during distribution of a tracer, and the choice of an E value is by no means unambiguous. The fact that the reported values of the perfusion reserve index, calculated with the assumption of a constant E, agree in normal healthy volunteers with previous PET studies is not sufficient to validate the application of the Kety model in patients.

Although Cullen et al. (1) describe their MRI measurements as first-pass studies, this does not seem to be appropriate when images are acquired every six heart beats. In fact, the Kety model may not fit well with data acquired in a true first-pass study owing to the initially low extraction of contrast agent during wash-in. The authors' criticism (p. 1391) of previous first-pass studies (6) because of use of a fast bolus injection is misleading. The perfusion reserve estimate obtained in patients with microvascular dysfunction with such MRI first-pass studies was validated by comparison to the coronary flow reserve (6). It remains to be shown that a perfusion reserve index derived with the Kety model corresponds under different pathophysiological conditions to the myocardial blood flow reserve. In our opinion the first-pass technique is preferred to determine myocardial blood flow and the myocardial blood flow reserve.

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REPLY

I would like to respond to several issues raised by the letter of Jerosch-Herold et al. First, I do not purport that a lower temporal resolution of an image every six heart beats used in our study (1) confers an advantage. This is a clear compromise between having more slices and less data points on the first-pass transit curves, which was necessitated by the hardware constraints we had at the inception of this study. Although the use of an inversion-recovery sequence results in relatively prolonged image acquisition times even with the fastest magnetic resonance imaging (MRI) scanners, the images are stable and of good quality for analysis. This is in contrast to the saturation-recovery sequences used by Jerosch-Herold (2), which may allow more of the heart to be imaged in less time but in which the images are often of poor quality and subject to artefacts. However, the slower injection technique used in our study is an advantage over the power injections into the right subclavian vein reported in other studies (2); this is because a relatively invasive subclavian line is needed, which is less attractive for patient and operator. Also, a power injector is required, which is safe with magnetic fields and correspondingly expensive, whereas our technique can be administered manually through a peripheral vein.

Second, the question of whether the extraction efficiency (E) remains constant or varies with myocardial flow (F) is controversial and as yet remains a subject for further research. In support of using the EF product (K_1) for estimating flow, a recent study by Vallee et al. (3) in a canine occluded coronary artery model demonstrated that F measured with microspheres had a linear fit to K_1 for Gd-DTPA, ($r = 0.88$). However, as the behavior of E is uncertain at differing flow rates, the term "myocardial perfusion